Cardiovascular morbidity and mortality among hypertensive patients in general practice: the evaluation of long-term systematic management

Harms, L.M.; Schellevis, F.G.; van Eijk, J.T.M.; Donker, A.J.M.; Bouter, L.M.

published in
Journal of Clinical Epidemiology
1997

DOI (link to publisher)
10.1016/S0895-4356(97)00066-8

document version
Publisher's PDF, also known as Version of record

J Clin Epidemiol Vol. 50, No. 7, pp. 779–786, 1997

ELSEVIER

0895-4356/97/$17.00
PII S0895-4356(97)00066-8

Cardiovascular Morbidity and Mortality Among Hypertensive Patients in General Practice: The Evaluation of Long-Term Systematic Management

L. M. Harms,[1,2,*] *F. G. Schellevis,*[1,2] *J. Th. M. van Eijk,*[1,2] *A. J. M. Donker,*[3] *and L. M. Bouter*[2,4]

[1]Department of General Practice, Nursing Home Medicine and Social Medicine; [2]Institute for Research in Extramural Medicine; [3]Institute for Cardiovascular Research; and [4]Department of Epidemiology and Biostatistics, Vrije Universiteit, Amsterdam, The Netherlands

ABSTRACT. *Objective*: To evaluate systematic management of hypertensive patients with regard to cardiovascular morbidity and mortality. *Design*: In a matched cohort study (1978–1993) the number of cardiovascular events among hypertensive patients under continuous systematic management in four general practices was compared with those occurring among hypertensive patients from eight "usual care" general practices. *Subjects*: The source population consisted of employees of a major electronic company in Eindhoven with hypertension as determined at an occupational health examination. The index group (n = 120) consisted of employees who were participating in the systematic management program in four practices. A reference group of 120 patients was selected from hypertensive employees who were registered in eight "usual care" practices by matching for age, gender, fasting blood glucose, and frequency of occupational health examinations. The total cohort consisted primarily of males (78%), whose ages ranged from 50 to 65 years. *Main outcome measures*: Risk difference (RD) per 1000 patient years regarding left ventricular hypertrophy, heart failure, angina pectoris, myocardial infarction, transient ischaemic attack, stroke, peripheral arterial disease, nephropathy, retinopathy, cardiac death, death due to stroke, and non-cardiovascular death was determined. In addition to morbidity and mortality, systematic hypertension management was evaluated with regard to cardiovascular risk factors throughout a period of maximally 12 successive years (1978–1989). Morbidity and mortality data were derived from general practice records and archives; data on risk factors were assessed at bi-annual occupational health examinations. *Results*: The total follow-up duration amounted to 2628 patient years. The mean follow-up duration in the index group was 10.8, in the reference group 11.1 years. As compared to the "usual care" reference group, the index group showed less left ventricular hypertrophy (RD 8.2, 95% CI 1.4–15.0), less angina pectoris (RD 9.7, 95% CI 2.0–17.4) and less peripheral arterial disease (RD 3.7, 95% CI 0.5–7.1). The difference in mean decrease in blood pressure during follow-up was 11.3 mmHg systolic and 5.9 mmHg diastolic in favour of the index group. No significant differences between the index and the reference groups were found with regard to the changes in other risk factors. *Conclusion*: In our study systematic management of hypertensive patients aged 50 to 65 in general practice was associated with a statistically significant, and clinically relevant decrease in cardiovascular morbidity and blood pressure. Although causality cannot be determined from this non-randomized cohort study, the findings do support the view that systematic management of hypertensive patients in general practice is valuable. J Clin Epidemiol 50;7:779–786, 1997. © 1997 Elsevier Science Inc.

KEY WORDS. Hypertension, morbidity, mortality, risk factors, management, general practice

INTRODUCTION

Hypertension is one of the principal risk factors associated with cardiovascular disease [1,2]. The success of short-term interventions with drug treatment in hypertensive patients has already been shown convincingly [3]. Interestingly, the most spectacular results of these studies were obtained among elderly [4]. However, the outcome of systematic management of hypertensive patients in general practice has been studied much less, and long-term studies in this field in particular are rare.

General practitioners (GPs) in The Netherlands are in a good position to implement prevention of cardiovascular disease, as are those in the United Kingdom [5,6]. The continuity of care, the fixed practice list of Dutch GPs, and the low threshold on the part of patients to consult GPs give

*Address for correspondence: L. M. Harms, M.D. Ph.D., Institute for Research in Extramural Medicine, Vrije Universiteit, van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands.

Accepted for publication on 8 April 1997.

them the opportunity to detect, treat, and follow patients who have a high risk for cardiovascular diseases. Systematic management involves surveillance and treatment of several risk factors, as well as of established cardiovascular disease.

In 1978, four general practitioners in Eindhoven (The Netherlands) started a systematic hypertension management program, including detection, treatment, and long-term management of hypertension. Systematic registration of patient data was an essential element of this program. As a substantial number of patients were employees of a local major electronic company with periodic occupational health examinations, also independent and standardized data on these patients are available. Because this company is the major employer in the region, it was also possible to identify a large reference group of hypertensive patients who were not registered in these four practices. This unique situation has led us to examine the following questions: (i) Are there differences in cardiovascular morbidity and mortality between hypertensive patients under systematic management and hypertensive patients under usual general practice care? (ii) What are the differences in time course of cardiovascular risk factors between both groups?

METHODS

Design

This article reports on a follow-up study among two subcohorts: an index and a reference group of hypertensive patients. The index group was characterized by participation in a systematic management program for hypertensive patients. The reference group receiving "usual care" for hypertension was established by matching. The number of cardiovascular events and the time course of cardiovascular risk factors was compared between these two groups. Cardiovascular events were measured over the period 1978–1993, measurements of risk factors took place during 1978–1988.

Patient Selection

Since 1977, all employees of a major electronic company in Eindhoven (The Netherlands) aged 50 to 65 have been invited to undergo a standardized occupational health examination every two years. Employees were considered to be hypertensive when they answered "yes" on the question "Do you use medication, do you have a diet, or are you being treated otherwise for hypertension?" or when they had a diastolic blood pressure (DBP) > 90 mmHg at one occasion during an occupational health examination. As additional eligibility criterium, at least one other occupational health examination must have taken place after the examination in which the hypertensive status was determined to have minimal information about the time course of risk factors. From this source population of hypertensive patients an index and a reference group was selected.

The index group consisted of all eligible patients registered in one of four general practices who participated in the systematic management program. This turned out to be the case for 191 patients. Of these, 62 patients never entered in the systematic management program because their blood pressure values never reached the entry criteria of the program. Of the 129 patients who did participate, the outcome data of 8 patients could not be traced; seven could not be traced due to a change of address or of general practitioner; and for 1 patient, no such data could be found. Finally, one patient was excluded because of secondary hypertension, which left 120 patients in the index group.

An equally sized reference group ($n = 120$) was established by matching the index group with hypertensive employees from the source population who were registered in eight other general practices who were not participating in the systematic management program. The following matching criteria were applied as measured at the first occupational health examination for the subject at issue after 1977: age group (50–54, 55–59, 60 and over), gender, fasting blood glucose level (<6.7 mmol/l or ≥6.7 mmol/l), and frequency of participation in the occupational health examinations (2, 3, 4 times or more). In case of more than one fitting match, selection was carried out at random.

Because of the followed selection procedure, the index group will probably include more truly and/or severely hypertensive patients, due to the additional inclusion criterium of participating in the systematic management program, than the reference group, which was selected solely on the basis of reporting hypertension in a questionnaire or a single blood pressure measurement.

Systematic Management Program

The systematic management program for hypertensive patients, which started in 1978, included detailed guidelines for GPs on detection, diagnostic procedures, non-medical and medical treatment, and monitoring of hypertension (see Appendix 1).

Variables and Measurements

OUTCOME VARIABLES. The following *cardiovascular morbidity and mortality* events (research question 1) were considered: myocardial infarction, angina pectoris, stroke, heart failure, peripheral arterial disease, nephropathy, retinopathy, cardiac death due to myocardial infarction (including sudden death), death due to heart failure, death due to stroke, and non-cardiovascular death. The occurrence of these events was derived from the patient records of the GPs and the GPs' archives of specialists' reports. In the case of morbidity, only events that were diagnosed by a specialist were taken into account. For this, it was necessary that the patient was referred to a specialist and that the GP had a

letter from the specialist in the patient's file. Moreover, these diagnoses were verified by comparing the information in the specialist's letter with the inclusion criteria of the International Classification of Health Problems in Primary Care (ICHPPC)-2 Defined [7] (see Appendix 2). In the case of mortality, the cause of death as recorded by the physician responsible for the care was accepted.

Cardiovascular morbidity also included left ventricular hypertrophy (LVH), which was determined according to ECG criteria. A six-channel ECG at rest was performed at each occupational health examination. Throughout the whole period, the ECGs were interpreted consecutively by three cardiologists in the ongoing operation of the occupational examinations. The ECGs were presented anonymously, so the cardiologist did not know whether the employee participated in the systematic management program. LVH was determined according to the Minnesota code [8] (LVH on the basis of voltage criteria only or with repolarization abnormalities). People with intraventricular condition disturbances (bundle branch block, ventricular block) were excluded for determining LVH. Only incident cases of LVH were considered, not showing LVH on their initial ECG.

A test–retest procedure was used to measure the inter-observer–reliability of the interpretation of the data on the events (occurrence of event and month/year of occurrence). For this purpose, a random sample of 10% was taken from the cohort. The outcome data on these 24 patients were interpreted by three medically qualified research-assistants. According to their assessment, a proportion of agreement of 97% was obtained on 22 items per patient (mean Cohen's kappa 0.82).

The following *cardiovascular risk factors* (research question 2) were studied: systolic and diastolic blood pressure, obesity, levels of serum cholesterol, glucose, glomerular filtration rate (GFR), stress, physical exercise, alcohol intake, and smoking. All data on cardiovascular risk factors were collected during the bi-annual occupational health examinations under the same standardized conditions. Consequently, data were available for six measuring points at a maximum. Blood pressure was measured by means of a mercury sphygmomanometer. The cuff size was 14 × 40 cm. The diastolic blood pressure was read at the disappearance of the Korotkoff tones (phase V). Obesity was defined as Body Mass Index (BMI) $\geq$ 30 kg/m^2. BMI was calculated using data on height and weight. The levels of total serum cholesterol, glucose, and creatinine were established by the same laboratory throughout the entire study. The limit values for increased total serum cholesterol ($\geq$8.0 mmol/l) and glucose ($\geq$7.0 mmol/l) were chosen according to the ICHPPC-2 diagnostic criteria [7]. The GFR was calculated by means of the Cockcroft and Gault's equation [9].

The questionnaire measuring stress, physical exercise, alcohol intake, and smoking was administered routinely by specially trained assistants. The same questions were used during the whole study, originating from a standardized national questionnaire for periodical occupational health examinations. The 10 stress items were factor-analyzed; one factor indicated perceived stress, the other indicated stress by workload. For each of the two dimensions, a value for each measuring point was computed. The risk factor stress was expressed in percentages of patients with stress (represented by at least one positive item) on both dimensions separately. A physical exercise score was computed on the basis of answers on questions about daily activities with three categories: low, medium, and high activity. The physical exercise summary measure expresses the percentage of patients with low physical activity per group. Finally, answers on questions about alcohol intake and smoking were dichotomized, which yielded percentages of high tobacco and high alcohol consumers for each measuring point for both groups.

PUTATIVE CONFOUNDERS. Data on age, gender, socioeconomic status (SES; two classes were considered on the basis of income [high and low]), type of insurance, and positive cardiovascular family history (defined as occurrence of hypertension, myocardial infarction, cerebrovascular accident, and/or diabetes mellitus in parents or siblings before the age of 60) were obtained by standardized questionnaires at the occupational health examinations. The year of inclusion into the cohort, intervention on cardiovascular risk factors by an occupational medical officer (independent from the GP), practice size, and rates of referral to cardiologists of the practice in which the patient was registered were also regarded as potentially confounding variables. Therefore, also data on these variables were collected.

Data Analysis

The index and the reference groups were compared with regard to their baseline status. Second, a comparison was made of the number of events in the index group and the reference group. The risk difference (incidence density difference) was calculated and 95% confidence intervals were computed. The groups were also compared by means of survival analysis. The survival analysis was carried out according to the Kaplan-Meier method, and significance was tested according to the Log-Rank test. In addition, a Cox's proportional hazards analysis was performed to adjust for possible confounding. The moment of inclusion into the cohort was taken as each patient's starting point of this survival analysis. Patients who died before December 31, 1992 from a non-cardiovascular cause were considered as censored cases.

The differences in the time course of cardiovascular risk factors between the index and reference groups were analyzed by time series analyses for repeated measurements for each risk factor separately. For these analyses, six measuring points were considered; the first measuring point was the

TABLE 1. Baseline characteristics of the index and reference group (n = 240)

	Index group (n = 120)	Reference group (n = 120)
Age (years [mean SD])	51.8 (2.8)	51.7 (2.8)
Sex (% males)	78	78
Insurance type (% sick funds insurance)	83	79
Socioeconomic status (% high)	11	22
Anti-hypertensive treatment (% with medication)	17	19
Duration of hypertension (years [mean SD])	4.5 (4.2)	3.4 (4.8)
Duration of follow-up (years [mean SD])	10.8 (3.7)	11.1 (3.7)
Systolic blood pressure (mmHg [mean SD])	164 (20)	148 (21)
Diastolic blood pressure (mmHg [mean SD])	103 (11)	95 (11)
Family history of hypertension (% positive)	31	17
Family history of myocardial infarction (% positive)	11	10
Family history of stroke (% positive)	8	5
Family history of diabetes mellitus (% positive)	6	8
Smoking status (% smokers)	53	44
Cholesterol (% with ≥ 8 mmol/l)	11	10
Fasting blood glucose (% with ≥ 7 mmol/l)	2	0
Body mass index (% with ≥ 30 kg/m^2)	14	13
Existing cardiovascular disease (% positive)	5	4
Glomerular filtration rate (ml/min [mean SD])	91 (15)	95 (19)

moment of inclusion into the cohort. Statistical significance was tested using Student's t-test for paired group means, and chi-square test for proportions.

RESULTS

Comparability of the Index and the Reference Group

Table 1 shows the baseline characteristics of the two groups. The mean duration of hypertension was 4.5 years for the index group, and 3.4 years for the reference group. Substantial differences between the two groups were found for SES, family history of hypertension, baseline blood pressure, and GFR. The baseline blood pressure was clearly higher in the index group (164/103 SBP/DBP mmHg) than in the reference group (148/95 SBP/DBP mmHg). The reference group consisted of more patients of high socioeconomic status and fewer patients with a positive family history of hypertension, and revealed on average, a higher GFR. SES, family history of hypertension, baseline blood pressure, and GFR were taken into account in the survival analysis. There were no differences between the two groups with regard to the year of inclusion into the cohort, the number of interventions by occupational medical officers, the number of referrals to cardiologists, and the size of the practice populations in which they were registered.

Events

The differences between the index and the references group with regard to morbidity and mortality are presented in Table 2. Total morbidity and mortality in 2628 patient years was significantly higher in the reference group. As compared with the reference group, there were fewer cases in the index group of left ventricular hypertrophy, angina pectoris, and peripheral arterial disease.

Survival analysis revealed that during the entire follow-up period, the proportion of patients with an event was higher in the reference group than in the index group (Fig. 1). In the Cox's proportional hazards model, SES, baseline blood pressure, GFR, and family history of hypertension were not significantly related to the occurrence of events (data not shown).

Risk Factors

The systolic and diastolic blood pressure in the index group fell significantly below that of the reference group (Fig. 2). The difference in mean fall of the systolic and diastolic blood pressure between the two groups during follow-up came to 11.3/5.9 mmHg (t-test, p = 0.002). The decrease in the proportion of patients with other risk factors (serum cholesterol ≥ 8 mmol/l, glucose ≥ 7 mmol/l, BMI ≥ 30 kg/m^2, stress, inactivity, and high alcohol consumption) was consistently larger in the index group than in the reference group but did not reach statistical significance (data not shown). In the index group 10% quitted smoking as opposed to 5% in the reference group (difference not significant).

DISCUSSION

This cohort study demonstrates that more than 10 years of systematic management of hypertensive patients, i.e., systematic treatment and follow-up in general practice, is asso-

TABLE 2. Morbidity and mortality for the index and the reference group (n = 240)

	Index group (1302 pt-yrs) n (abs)	Reference group (1326 pt-yrs) n (abs)	Risk difference[a] per 1000 pt-yrs (95% CI)
Morbidity			
Left ventricular hypertrophy	5	16	8.2 (1.4–15.0)
Heart failure	2	2	0.0 (−3.0–3.0)
Angina pectoris	7	20	9.7 (2.0–17.4)
Myocardial infarction	11	15	2.9 (−4.7–10.4)
Stroke	3	5	1.5 (−2.7–5.7)
Transient ischaemic attack	1	4	2.3 (−1.1–5.6)
Peripheral arterial disease	0	5	3.7 (0.5–7.1)
Retinopathy	4	5	0.7 (−3.8–5.2)
Nephropathy	0	1	0.8 (−0.7–2.2)
Mortality			
Death due to stroke	0	2	1.5 (−0.6–3.6)
Cardiac death	5	6	0.7 (−4.3–5.6)
Total cardiovascular death	5	8	2.2 (−3.2–7.6)
Non-cardiovascular death	8	7	−0.9 (−6.6–4.9)
Number of patients with ≥1 event	27	55	23.0 (9.7–36.3)

Abbreviations: abs = absolute number; pt-yrs = patient-years.
[a]Incidence density difference between reference and index group.

ciated with lower cardiovascular morbidity rates as compared with usual care, as well as with a larger decrease in systolic and diastolic blood pressure in patients aged 50 to 65 years. Unlike blood pressure, the differences between the index and the reference groups with regard to other risk factors such as increased total serum cholesterol, obesity, and smoking, were not significant.

A significant difference with regard to the incidence of angina pectoris in relation with antihypertensive treatment has to our knowledge not been described before. The most positive results of antihypertensive treatment on coronary morbidity, and mortality were found in studies on older male patients with a relatively long follow-up [4,10,11]. These studies, however, were not carried out in a general practice setting. Apparently, reduction of coronary morbidity and mortality can only be found in a population with a

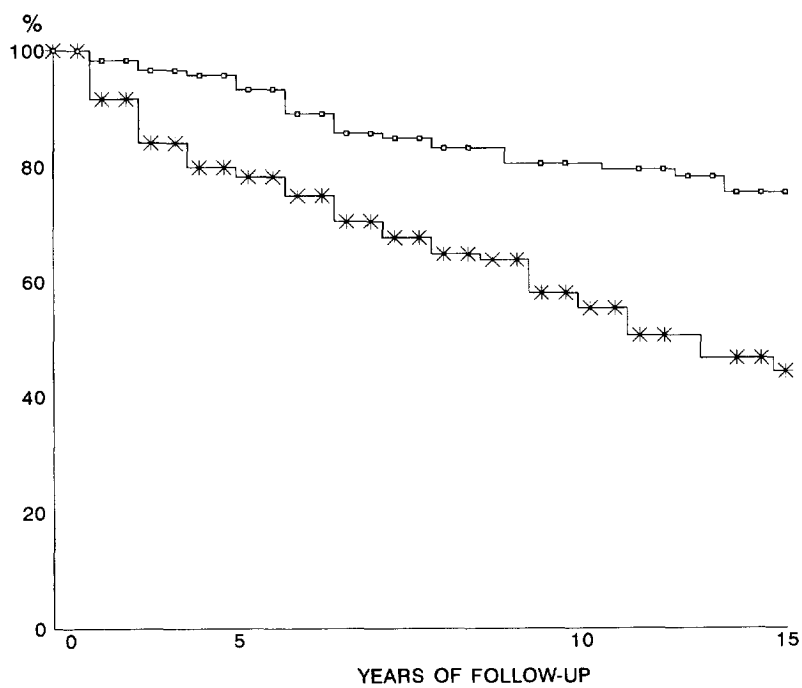

FIGURE 1. Proportions of patients in index and reference group without cardiovascular events during 15 years of follow-up. Survival analysis (n = 240). Legend: index group (*squares*), reference group (*asterisks*). Log-rank test: p = 0.0005.

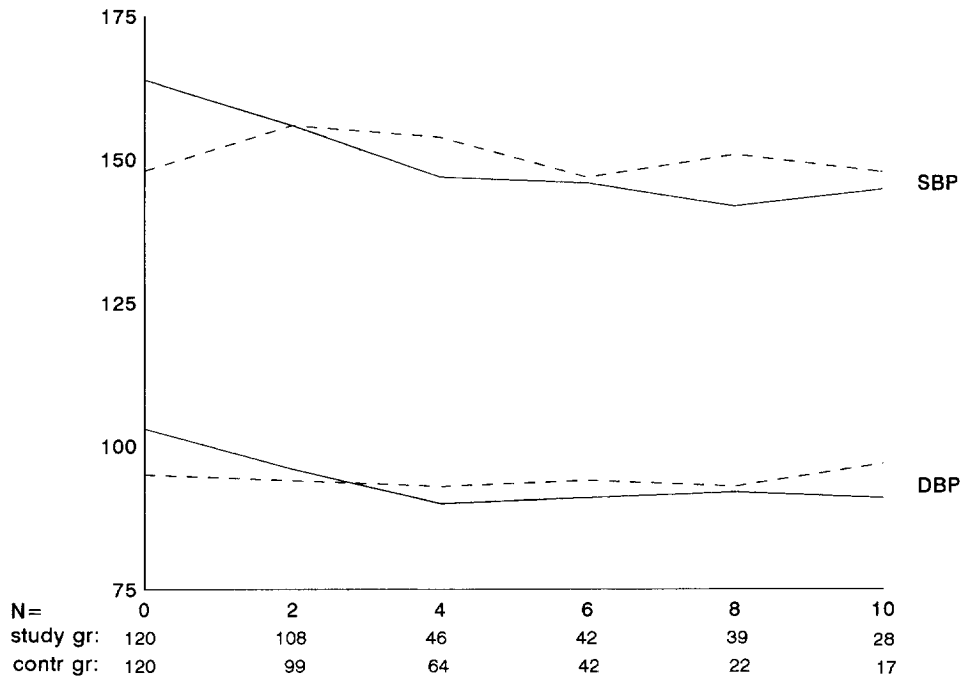

FIGURE 2. Mean systolic and diastolic blood pressure of index and reference group during follow-up (n = 240). Legend: index group (*solid lines*), reference group (*dashed lines*). Student's test: p = 0.002.

high incidence of these events, i.e., in male elderly patients during a long follow-up, as was the case in our study. The large Medical Research Council (MRC) trial, for example, was conducted in younger patients with about as many males as females, and did not show differences for coronary events [12]. Our study demonstrated especially differences among "soft" cardiovascular outcomes as LVH and angina pectoris. This could possibly be explained by a preventive influence of our program on atherosclerosis. Other studies [2,3] with a mean follow-up of five years showed differences in "hard" cardiovascular outcomes as myocardial infarction and stroke, which are events following more advanced stages of atherosclerosis. Another explanation for these discrepancies between our results and those of other studies is the influence of risk factors, especially hyperlipidaemia [13,14]. Our program took other important risk factors, such as smoking and hypercholesterolaemia, into account and we found a non-significant trend toward a lower proportion of patients with risk factors in the index group during follow-up. In the MRFIT study, which also included a multifactor approach, statistically significant differences were found on seven-year incidence rates of, among others, angina pectoris, peripheral arterial disease [15]. These results, regarding 35–57-year-old males and a follow-up duration of seven years, are in line with our hypotheses mentioned above.

We were impressed by the high number of patients with one or more events in the reference group in our study. However, compared with a similar group of hypertensive males, aged 50–65, the figures seem not to be abnormal [16]. Moreover, it is important to stress that LVH usually is not included in studies on cardiovascular diseases.

A possible source of confounding of the results is a selective inclusion by the GPs of hypertensive patients in the systematic management program, for example relatively more compliant, less severe, highly motivated patients. As mentioned above, the index group probably contained more truly hypertensive patients than the reference group due to the selection procedure. This would implicate that the observed differences in morbidity and mortality between the two groups possibly represent an underestimation of the differences that would occur when the reference group would have consisted of only truly hypertensives at high risk for cardiovascular morbidity and mortality.

The data on the cardiovascular events were derived from the GP records and information in specialists' reports. Obviously, the GPs of the four practices who participated in the systematic management program had a more active attitude toward their hypertensive patients compared with the GPs of the other practices. This could lead to more attention toward the detection of cardiovascular diseases. One could therefore hypothesize that the number of events in the reference group is underestimated. However, this also would indicate that our findings would underestimate the real influence of systematic management. The data on risk factors were collected during the occupational medical examinations by independent observers who had no information about participation in the systematic management program. Therefore, observer bias for these data can be excluded. Also, the referral rates to cardiologists of practices to which the index and the reference group belonged were similar during the entire follow-up period. Of course there is a possibility, however, that the two groups were incomparable to one another due to unknown but potentially confounding variables that would threaten the validity of our findings.

So far, our treatment of a population of middle-aged, primarily male hypertensive patients was associated with a lower number of cardiovascular events compared with a reference group. We acknowledge that our findings are improbable as they have never been demonstrated before. Although trying seriously we were not able to argue our findings away except for the argument of the non-randomized nature of our study. We hope that our results will challenge others to demonstrate, preferably by studies in randomized controlled settings, whether we are right or wrong. In the meantime, our findings support the view that systematic management of hypertensive patients in general practice is valuable.

The authors thank Mrs. D. Kriegsman, M.D., Ph.D. for her help in carrying out the survival analysis.

References

1. Castelli WP. Epidemiology of coronary heart disease: The Framingham Study. **Am J Med** 1984; 76: 4–12.
2. MacMahon S, Peto R, Cutler J, *et al.* Epidemiology, blood pressure, stroke and coronary heart disease. Part 1: Prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution bias. **Lancet** 1990; 335: 765–774.
3. Collins R, Peto R, MacMahon S, *et al.* Epidemiology, blood pressure, stroke and coronary heart disease. Part 2: Short-term reductions in blood pressure: Overview of randomized drug trials in their epidemiological context. **Lancet** 1990; 335: 827–838.
4. Dahlöf B, Lindholm LH, Hansson, *et al.* Morbidity and mortality in the Swedish Trial in old patients with hypertension (STOP-Hypertension). **Lancet** 1991; 338: 1281–1284.
5. D'Souza MF, Swan AV, Shannon DJ. A long-term controlled trial of screening for hypertension in general practice. **Lancet** 1976; i: 1228–1283.
6. Heller R, Rose G. Current management of hypertension in general practice. **Br Med J** 1977; i: 1442–1444.
7. Classification Committee of WONCA. **International Classification of Health Problems in Primary Care (ICHPPC)-2-Defined.** Oxford: Oxford University Press; 1983.
8. Prineas RJ, Crow RS, Blackburn H. **The Minnesota Code Manual of Electrocardiographic Findings—Standards and Procedures for Measurement and Classification.** Littleton: Wright-PSG; 1982.
9. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. **Nephron** 1976; 16: 31–41.
10. Améry A, Birkenhäger W, Brixko P, *et al.* Mortality and morbidity results from the European working party on high blood pressure in the elderly trial. **Lancet** 1985; i: 1349–1354.
11. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. **J Am Med Assoc** 1991; 265: 3255–3264.
12. Medical Research Council Working Party. MRC-trial of treatment of mild hypertension: Principal results. **Br Med J** 1985; 291: 97–104.
13. Strangaard S. Why does antihypertensive treatment prevent stroke but not myocardial infarction. **Lancet** 1987; ii: 658–661.
14. Lindholm LH. Cardiovascular risk factors and their interactions in hypertensives. **J Hypert** 1991; 9: S3–S6.
15. Multiple Risk Factor Intervention Trial Research Group. Coronary heart disease death, nonfatal acute myocardial infarction and other clinical outcomes in the Multiple Risk Factor Intervention Trial. **Am J Cardiol** 1986; 58: 1–13.
16. Sytkowksi PA, Kannel WB, d'Agostino RB. Changes in risk factors and the decline in mortality from cardiovascular disease. The Framingham Heart Study. **N Engl J Med** 1990; 322: 1635–1641.

APPENDIX 1
The Systematic Management Program

After a phase of "case-finding" of hypertensive patients, four general practices in Eindhoven, The Netherlands, have conducted a systematic management of hypertensive patients since 1978 in accordance with a fixed protocol. The objective of this surveillance was to prevent cardiovascular diseases by restoring normotension (diastolic blood pressure ≤ 90 mmHg), and reducing the level of other cardiovascular risk factors, in particular obesity, increased total serum cholesterol level, and smoking.

The care of the patients was provided according to strict guidelines. The GP was responsible for (1) compiling findings of hypertensive patients; (2) checking patients' blood pressure every three months; (3) scheduling a treatment ('stepped care'); (4) inviting patients to an annual examination (blood pressure, BMI, laboratory tests, ECG, and chest x-ray), carried out in a non-hospital based diagnostic center (apart from the GPs own practices); and (5) conducting compliance checks.

"Case-finding" refers to the practice of measuring blood pressure of every patient over the age of 20 during consultation hours who (1) had a personal history of cardiovascular disease; (2) had a positive family history of cardiovascular disease; or (3) was affected by other risk factors associated with cardiovascular disease (obesity, increased total cholesterol levels, smoking, and stress).

The term "stepped care" refers to treatment with a thiazide diuretic and/or beta-blocker at increasing doses, if necessary combined with a vasodilator.

APPENDIX 2
ICHPPC-2-Defined Diagnostic Criteria

MYOCARDIAL INFARCTION (ICHPPC-2 CODE 410-). Inclusion requires two of the following within eight weeks of onset: (1) chest pain characteristic of myocardial ischemia, lasting more than 15 minutes; (2) abnormal ST-T changes or Q-waves in electrocardiogram; and (3) elevation of blood cardiac enzymes.

ANGINA PECTORIS (ICHPPC-2 CODE 412-). Inclusion requires one of the following: (1) chest pain compatible with angina pectoris; (2) demonstration of myocardial ischemia by resting or exercise ECG; and (3) X-ray evidence of coronary artery narrowing.

STROKE (ICHPPC-2 CODE 438-). Signs and symptoms of a disturbance of cerebral function, presumed of vascular origin, lasting more than 24 hours or causing death.

HEART FAILURE (ICHPPC-2 CODE 428-). Inclusion requires three of the following: (1) dependent edema; (2) raised jugular venous pressure or hepatomegaly in the absence of liver disease; (3) signs

of pulmonary congestion or pleural effusion; (4) enlarged heart; and (5) dyspnea in the absence of pulmonary disease.

PERIPHERAL ARTERIAL DISEASE (ICHPPC-2 CODE 443-). Inclusion requires one of the following: (1) signs or symptoms of tissue ischemia due to obstruction of an artery; and (2) investigative evidence of arterial obstruction.

NEPHROPATHY/RETINOPATHY (ICHPPC-2 CODE 402-). Inclusion requires both the following: (1) blood pressure levels meeting the criteria for hypertension; (2) abnormalities of the kidney (albuminuria, azotemia) or fundus attributed to hypertension.